

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
17 February 2005 (17.02.2005)

PCT

(10) International Publication Number  
**WO 2005/014517 A3**

(51) International Patent Classification<sup>7</sup>: **C07C 235/40**,  
C07D 313/14, 267/20, A61K 31/335, 31/395, 31/165,  
A61P 25/28

(21) International Application Number:  
PCT/EP2004/008283

(22) International Filing Date: 23 July 2004 (23.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0317491.9 25 July 2003 (25.07.2003) GB

(71) Applicant (for all designated States except AT, US): **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(71) Applicant (for AT only): **NOVARTIS PHARMA GMBH** [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **AUBERSON, Yves** [CH/CH]; Maiengasse 4, CH-4123 Allschwil (CH). **BETSCHART, Claudia** [CH/CH]; In den Ziegelhöfen 93, CH-4054 Basel (CH). **FLOHR, Stefanie** [DE/CH]; St. Galler Ring 142, CH-4054 Basel (CH). **GLATTHAR, Ralf** [DE/DE]; Badmatte 5, 79713 Bad Säckingen (DE). **SIMIC, Oliver** [DE/CH]; Gundeldingerstrasse 209, CH-4053 Basel (CH). **TINTELNOT-BLOMLEY, Marina** [DE/DE]; Roettlerstrasse 1, 79689 Maulburg

(DE). **TROXLER, Thomas, J.** [CH/CH]; Sennweg 27, CH-4246 Wahlen (CH). **VANGREVELINGHE, Eric** [FR/FR]; 41, rue de Saint-Louis, F-68330 Huningue (FR). **VEENSTRA, Siem, Jacob** [NL/DE]; Rebweg 28, 79540 Lörrach (DE).

(74) Agent: **GRUBB, Philip**; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

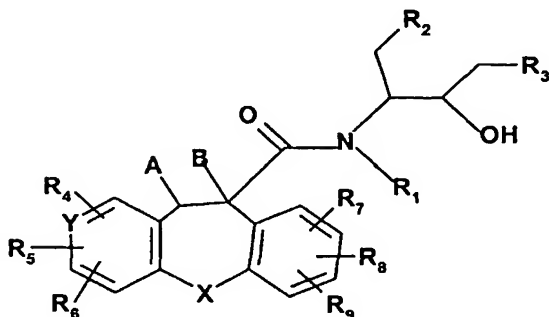
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

[Continued on next page]

(54) Title: **NOVEL DIBENZO[B,F]OXEPINE-10-CARBOXAMIDES AND PHARMACEUTICAL USES THEREOF**



(I)

(57) Abstract: The present invention pertains to compounds of formula (I) wherein X is O, NH, N(C<sub>1-4</sub>)alkyl, CO or CHO, Y is CH or N, A and B are each hydrogen or together form a second bond between the carbon atoms to which they are attached, R<sub>1</sub> is hydrogen or (C<sub>1-4</sub>)alkyl, R<sub>2</sub> is optionally substituted (C<sub>1-8</sub>)alkyl, (C<sub>3-7</sub>)cycloalkyl, (C<sub>3-7</sub>)cycloalkyl(C<sub>1-4</sub>)alkyl, aryl or heteroaryl, R<sub>3</sub> is CH(R<sub>c</sub>)CONR<sub>a</sub>R<sub>b</sub> or (CH<sub>2</sub>)<sub>n</sub>NR<sub>c</sub>R<sub>d</sub>, n is 0, 1 or 2, R<sub>a</sub>, R<sub>b</sub>, R<sub>c</sub> and R<sub>d</sub>, independently, are hydrogen or optionally substituted (C<sub>1-8</sub>)alkyl, (C<sub>3-7</sub>)cycloalkyl, (C<sub>3-7</sub>)cycloalkyl(C<sub>1-4</sub>)alkyl, (C<sub>7-9</sub>)bicycloalkyl,

1-aza-(C<sub>7-9</sub>)bicycloalkyl, aryl, aryl(C<sub>1-4</sub>)alkyl, heteroaryl, heteroaryl(C<sub>1-4</sub>)alkyl or heterocyclyl, or R<sub>a</sub>, R<sub>b</sub>, R<sub>c</sub> and R<sub>d</sub>, together with the nitrogen to which they are attached, form an optionally substituted pyrrolidinyl, piperidino, morpholino or piperazinyl group, R<sub>c</sub> is (C<sub>1-8</sub>)alkyl, (C<sub>1-4</sub>)alkoxy(C<sub>1-4</sub>)alkyl, (C<sub>3-7</sub>)cycloalkyl or (C<sub>3-7</sub>)cycloalkyl(C<sub>1-4</sub>)alkyl, and R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub>, independently, are hydrogen, (C<sub>1-4</sub>)alkyl, (C<sub>1-4</sub>)alkoxy, (C<sub>1-4</sub>)alkyl-SO<sub>2</sub>, cyano, nitro or halogen; to a process for the preparation of such compounds of formula (I), their use as pharmaceuticals, especially in the treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation, and to pharmaceutical compositions and combinations comprising such compounds of formula (I).



**(88) Date of publication of the international search report:**  
28 April 2005

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*